

**We claim:**

1. A method of treating or preventing chronic renal failure in a mammal, comprising conjointly administering to said mammal an OP/BMP morphogen and an Angiotensin-Converting Enzyme Inhibitor (ACEI).
- 5 2. A method of treating or preventing chronic renal failure in a mammal, comprising conjointly administering to said mammal an OP/BMP morphogen and an Angiotensin II Receptor Antagonist (AIIRA).
3. A method of treating or preventing chronic renal failure in a mammal, comprising conjointly administering to said mammal an inducer of  
10 endogenous OP/BMP morphogen expression and an Angiotensin-Converting Enzyme Inhibitor (ACEI).
4. A method of treating or preventing chronic renal failure in a mammal, comprising conjointly administering to said mammal an inducer of  
15 endogenous OP/BMP morphogen expression and an Angiotensin II Receptor Antagonist (AIIRA).
5. A method of treating or preventing chronic renal failure in a mammal, comprising conjointly administering to said mammal an agonist of an OP/BMP morphogen receptor and an Angiotensin-Converting Enzyme Inhibitor (ACEI).
- 20 6. A method of treating or preventing chronic renal failure in a mammal, comprising conjointly administering to said mammal an agonist of an OP/BMP morphogen receptor and an Angiotensin II Receptor Antagonist (AIIRA).
- 25 7. A method of treating or preventing chronic renal failure in a mammal, comprising introducing into the kidney of said mammal a therapeutically effective amount of renal mesenchymal progenitor cells pre-treated

conjointly with an ACEI and an agent that increases the abundance of an OP/BMP morphogen.

8. A method of treating or preventing chronic renal failure in a mammal, comprising introducing into the kidney of said mammal a therapeutically effective amount of renal mesenchymal progenitor cells pre-treated conjointly with an AIIRA and an agent that increases the abundance of an OP/BMP morphogen.
9. The method of claim 7 or 8, wherein the agent is an OP/BMP morphogen.
10. The method of claim 7 or 8, wherein the agent is an inducer of an OP/BMP morphogen.
11. The method of claim 7 or 8, wherein the agent is an agonist of an OP/BMP morphogen receptor.
12. A method for delaying the need for, or reducing the frequency of, chronic dialysis treatments, comprising conjointly administering to a mammal an OP/BMP morphogen and an ACEI.
13. A method for delaying the need for, or reducing the frequency of, chronic dialysis treatments, comprising conjointly administering to a mammal an OP/BMP morphogen and an AIIRA.
14. A method for delaying the need for, or reducing the frequency of, chronic dialysis treatments, comprising conjointly administering to said mammal an inducer of endogenous OP/BMP morphogen expression and an ACEI.
15. A method for delaying the need for, or reducing the frequency of, chronic dialysis treatments, comprising conjointly administering to said mammal an inducer of endogenous OP/BMP morphogen expression and an AIIRA.
16. A method for delaying the need for, or reducing the frequency of, chronic dialysis treatments, comprising conjointly administering to said mammal an agonist of an OP/BMP morphogen receptor and an ACEI.

17. A method for delaying the need for, or reducing the frequency of, chronic dialysis treatments, comprising conjointly administering to said mammal an agonist of an OP/BMP morphogen receptor and an AIIRA.
- 5 18. A method as in any one of claims 1-17, wherein said mammal is afflicted with a condition selected from: chronic renal failure (CRF), end-stage renal disease (ESRD), chronic diabetic nephropathy, diabetic glomerulopathy, diabetic renal hypertrophy, hypertensive nephrosclerosis, hypertensive glomerulosclerosis, chronic glomerulonephritis, hereditary nephritis, or renal dysplasia.
- 10 19. A method as in any one of claims 1-17, wherein examination of a renal biopsy of said mammal indicates that said mammal is afflicted with a condition selected from: glomerular hypertrophy, tubular hypertrophy, glomerulosclerosis, or tubulo interstitial sclerosis.
- 15 20. A method as in any one of claims 1-17, wherein examination of said mammal indicates renal fibrosis.
21. The method of claim 20, wherein said examination is an ultrasound, NMR or CAT scan of said mammal.
22. A method as in any one of claims 1-17, wherein said mammal possesses a number of functional nephron units which is less than about 40% of a number of functional nephron units present in a mammal having intact healthy kidneys.
- 20 23. The method of claim 22, wherein said mammal possesses a number of functional nephron units which is less than about 20% of a number of functional nephron units present in a mammal having intact healthy kidneys.
- 25 24. The method of any one of claims 1-17, wherein said mammal is a kidney transplant recipient.

25. The method of any one of claims 1-17, wherein said mammal possesses only one kidney.
26. The method of any one of claims 1-17, wherein examination of a urinary sediment of said mammal indicates a presence of broad casts.
- 5 27. The method of any one of claims 1-17, wherein said mammal has a GFR which is chronically less than about 40% of a  $GFR_{exp}$  for said mammal.
28. The method of claim 27, wherein said mammal has a GFR which is chronically less than about 20% of a  $GFR_{exp}$  for said mammal.
- 10 29. The method of any one of claims 1-17, wherein said mammal is a human male weighing at least about 50 kg and has a GFR which is chronically less than about 40 ml/min.
30. The method of any one of claims 1-17, wherein said mammal is a human female weighing at least about 40 kg and has a GFR which is chronically less than about 30 ml/min.
- 15 31. The method of any one of claims 1-17, wherein said treatment or prevention reduces serum creatinine levels in said mammal by at least about 5% over 3 months.
32. The method of any one of claims 1-17, wherein prior to said treatment or prevention, said mammal presented a chronic decline in a clinical indicator of renal function, and after at least about 3 months of said treatment or prevention, said indicator stabilizes.
- 20 33. The method of any one of claims 1-6 and 12-17, wherein at least one of said ACEI, said AIIRA or said morphogen is administered orally, parenterally, intravenously, intraperitoneally, or into a renal capsule, or by an implanted device.
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34. The method of claim 33, wherein a stent has been implanted into said mammal for said administration of at least one of said ACEI, said AIIRA or said morphogen.
- 5 35. The method of any one of claims 1-6 and 12-17, wherein at least one of said ACEI or said AIIRA, and at least one of said morphogen are conjointly administered at least once a week for a period of at least about one month.
36. The method of any one of claims 1-6 and 12-17, wherein at least one of said ACEI or AIIRA, and at least one of said morphogen are conjointly administered at least once a week for a period of at least about one year.
- 10 37. The method of any one of claims 1-6 and 12-17, wherein said ACEI or said AIIRA, and said morphogen are administered through different routes.
38. The method of any one of claims 1-6 and 12-17, wherein said ACEI or said AIIRA, and said morphogen are conjointly administered at different frequencies.
- 15 39. The method of any one of claims 1-6 and 12-17, wherein said morphogen is administered at a dosage of about 0.01-1000  $\mu\text{g/kg}$  body weight of said mammal.
40. The method of claim 39, wherein said morphogen is administered at a dosage of about 10-300  $\mu\text{g/kg}$  body weight of said mammal.
- 20 41. The method of any one of claims 1, 3, 5, 12, 14 and 16, wherein said ACEI is administered orally at a concentration of about 1-10,000 mg/L, preferably 10-1000 mg/L, 10-100 mg/L, 100-1000 mg/L, most preferably 100 mg/L.
42. The method of any one of claims 2, 4, 6, 13, 15 and 17, wherein said AIIRA is administered orally at a concentration of about 0.01-100 mg/kg body weight, preferably 0.1-10 mg/kg body weight, 0.2-5 mg/kg body weight, 0.5-25 2 mg/kg body weight, most preferably 1 mg/kg body weight.

43. The method of any one of claims 1-6 and 12-17, wherein said OP/BMP morphogen and, ACEI or AIIRA are administered in a single pharmaceutical composition.
- 5 44. The method of any one of claims 1-6 and 12-17, wherein said OP/BMP morphogen and, ACEI or AIIRA are administered in separate pharmaceutical compositions at or around the same time.
45. The method of any one of claims 1-6 and 12-17, wherein said OP/BMP morphogen and, ACEI or AIIRA are administered in separate pharmaceutical compositions at different times.
- 10 46. The method of any one of claims 1-17, wherein said morphogen (a) induces chondrogenesis in an ectopic bone assay; (b) prevents, inhibits, delays or alleviates loss of renal function in an animal model of chronic renal failure, or (c) causes a clinically significant improvement in a standard marker of renal function when administered to a mammal in, or at risk of, chronic renal failure.
- 15 47. The method of of any one of claims 1-17, wherein said morphogen comprises a polypeptide including at least a C-terminal cysteine domain of a protein selected from: a pro form, a mature form, or a soluble form of a polypeptide, wherein said polypeptide is: OP-1, OP-2, OP-3, BMP2, BMP3, BMP4, BMP5, BMP6, or BMP9.
- 20 48. The method of claim 47, wherein said morphogen comprises a polypeptide including at least a C-terminal cysteine domain of a polypeptide selected from: a pro form, a mature form, or a soluble form of human OP-1.
- 25 49. The method of claim 1, wherein said morphogen comprises a polypeptide having at least 70% homology or 50% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1 (SEQ ID NO: 2).

50. The method of claim 49, wherein said polypeptide has at least 75% homology or 60% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1 (SEQ ID NO: 2).
51. The method of claim 49, wherein said polypeptide has at least 80% homology or 70% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1 (SEQ ID NO: 2).
52. The method of claim 53, wherein said polypeptide has at least 90% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1 (SEQ ID NO: 2).
53. The method of any one of claims 1, 3, 5, 7, 9-12, 14, and 16, wherein said ACEI is: any one compound of the formulas I-XXVIII or their salts thereof; acylmercapto and mercaptoalkanoyl prolines; captopril (1-[(2S)-3-mercapto-2-methylpropionyl]-L-proline); ether or thioether mercaptoacyl prolines; zofenopril; carboxyalkyl dipeptides; enalapril (N-(1-ethoxycarbonyl-3-phenylpropyl)-L-ananyl-L-proline); lisinopril; quinapril; ramipril; carboxyalkyl dipeptide mimics; cilazapril; benazapril; phosphinylalkanoyl prolines; fosinopril;trandolopril; phosphonamidate substituted amino or imino acids; phosphonate substituted amino or imino acids and salts thereof; ceronapril ((S)-1-[6-amino-2-[[hydroxyl(4-phenylbutyl)phosphinyl]oxy]-1-oxohexyl]-L-proline); BRL 36,378; MC-838; CGS 14824 (3-([1-ethoxycarbonyl-3-phenyl-(1S)-propyl]-amino)-2,3,4,5-tetrahydro-2-oxo-1-(3S)-benzazepine-1 acetic acid HCL); CGS 16,617 (3(S)-[[[(1S)-5-amino-1-carboxypentyl]amino]2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-ethanoic acid); Cetapril (alacepril, Dainippon); Ru 44570; Cilazapril; Ro 31-2201; Lisinopril; Indalapril (delapril); Rentiapril (fentiapril, Santen); Indolapril; Spirapril; Perindopril; Quinapril; CI 925 ([3S-[2[R(\*)R(\*)]]3R(\*)]-2-[2-[[1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-3-isoquinolinecarboxylic acid HCL); WY-44221; mercapto-containing compounds; pivopril; YS980; Omapatrilat; Alacepril;

moveltopril; quinaprilat; moexipril; perinodpril (S-9490); pentopril;  
ancovenin; phenacein; or nicotianamin.

54. The method of any one of claims 2, 4, 6, 8-11, 13, 15, and 17, wherein said  
AIIRA is: Losartan (Cozaar<sup>®</sup>), Valsartan (Diovan<sup>®</sup>), Irbesartan (Avapro<sup>®</sup>),  
5 Candesartan (Atacand<sup>®</sup>), Telmisartan (Micardis<sup>®</sup>), tasosartan, zolarsartan,  
Teveten (eprosartan mesylate) or olmesartan medoxomil (Benicar).
55. The method of any one of claims 1, 3, 5, 7, 9-12, 14, and 16, wherein said  
ACEI is Enalapril.
56. A pharmaceutical composition comprising a therapeutically effective amount  
10 an ACE inhibitor and an OP/BMP morphogen formulated with  
pharmaceutically acceptable salt, carrier, excipient or diluent.
57. A pharmaceutical composition comprising a therapeutically effective amount  
an AIIRA and an OP/BMP morphogen formulated with pharmaceutically  
acceptable salt, carrier, excipient or diluent.
- 15 58. The pharmaceutical composition of claim 56, wherein the ACE inhibitor is  
Enalapril.
59. The pharmaceutical composition of claim 57, wherein the AIIRA is:  
Losartan (Cozaar<sup>®</sup>), Valsartan (Diovan<sup>®</sup>), Irbesartan (Avapro<sup>®</sup>), Candesartan  
(Atacand<sup>®</sup>), Telmisartan (Micardis<sup>®</sup>), tasosartan, zolarsartan, Teveten  
20 (eprosartan mesylate) or olmesartan medoxomil (Benicar).
60. The pharmaceutical composition of claim 56 or 57, wherein the morphogen  
is the polypeptide of SEQ ID NO: 3.
61. The pharmaceutical composition of claim 56 or 57, wherein the morphogen  
is a first polypeptide including at least a C-terminal cysteine domain of a  
25 protein selected from: a pro form, a mature form, or a soluble form of a  
second polypeptide, wherein said second polypeptide is: OP-1, OP-2, OP-3,  
BMP2, BMP3, BMP4, BMP5, BMP6, or BMP9.



62. The pharmaceutical composition of claim 56 or 57, wherein said morphogen comprises a polypeptide having at least 70% homology or 50% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1 (SEQ ID NO: 2).
- 5 63. The pharmaceutical composition of claim 62, wherein said polypeptide has at least 75% homology or 60% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1 (SEQ ID NO: 2).
64. The pharmaceutical composition of claim 62, wherein said polypeptide has at least 80% homology or 70% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1 (SEQ ID NO: 2).
- 10 65. The pharmaceutical composition of claim 62, wherein said polypeptide has at least 90% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1 (SEQ ID NO: 2).
66. The pharmaceutical composition of claim 56, wherein said ACEI is: any one compound of the formulas I-XXVIII or their salts thereof; acylmercapto and mercaptoalkanoyl prolines; captopril (1-[(2S)-3-mercapto-2-methylpropionyl]-L-proline); ether or thioether mercaptoacyl prolines; zofenopril; carboxyalkyl dipeptides; enalapril (N-(1-ethoxycarbonyl-3-phenylpropyl)-L-ananyl-L-proline); lisinopril; quinapril; ramipril;
- 15 20 carboxyalkyl dipeptide mimics; cilazapril; benazapril; phosphinylalkanoyl prolines; fosinopril;trandolopril; phosphonamidate substituted amino or imino acids; phosphonate substituted amino or imino acids and salts thereof; ceronapril ((S)-1-[6-amino-2-[[hydroxyl(4-phenylbutyl)phosphinyl]oxy]-1-oxohexyl]-L-proline); BRL 36,378; MC-838; CGS 14824 (3-([1-ethoxycarbonyl-3-phenyl-(1S)-propyl]-amino)-2,3,4,5-tetrahydro-2-oxo-1-(3S)-benzazepine-1 acetic acid HCL); CGS 16,617 (3(S)-[[[(1S)-5-amino-1-carboxypentyl]amino]2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-ethanoic acid); Cetapril (alacepril, Dainippon); Ru 44570; Cilazapril; Ro 31-2201; Lisinopril; Indalapril (delapril); Rentiapril (fentiapril, Santen); Indolapril;
- 25 30 Spirapril; Perindopril; Quinapril; CI 925 ([3S-[2[R(\*)R(\*)]]3R(\*)]-2-[2-[[1-

(ethoxy-carbonyl)-3-phenylpropyl]amino[-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-3-isoquinolinecarboxylic acid HCL); WY-44221; mercapto-containing compounds; pivopril; YS980; Omapatrilat; Alacepril; moveltopril; quinaprilat; moexipril; perinodpril (S-9490); pentopril; 5 ancovenin; phenacein; or nicotianamin.

67. The pharmaceutical composition of claim 57, wherein said AIIRA is: Losartan (Cozaar<sup>®</sup>), Valsartan (Diovan<sup>®</sup>), Irbesartan (Avapro<sup>®</sup>), Candesartan (Atacand<sup>®</sup>), Telmisartan (Micardis<sup>®</sup>), tasosartan, zolarsartan, Teveten (eprosartan mesylate) or olmesartan medoxomil (Benicar).
- 10 68. A package pharmaceutical comprising the pharmaceutical composition of any one of claims 56-67, in association with instructions for administering the composition to a mammal for treatment or prevention of chronic renal failure.